REMARKS/ARGUMENTS

Claims 44-61 are pending in this application, and claims 44-61 have been rejected.

Claim Rejections – 35 USC 112

Claims 44-58 have been rejected under 35 USC 112, second paragraph, as being indefinite or failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Applicant has amended claim 44, step d) to further clarify the analysis based on proportions of labeled malignant cells, and said labeled cell fragments or said labeled cellular debris over time as described in example (US20040181463, Page 13, Para 0137).

Applicant has amended claim 53, step c) to remove cell fragments/debris with no antecedent basis and include the clusters of malignant cells.

Applicant has amended claim 53, step d) to further clarify the analysis based on proportions of labeled malignant cells, and said labeled clusters over time

Claim Rejections – 35 USC 102

Claims 44-61 have been rejected under 35 USC 102(e) as being anticipated by Schmitz et al. (US Pat. No. 6,190,870).

Applicant has amended independent claims 44 and 53 to reflect the particle differences between Schmitz and the present invention with respect to the use of HGMS. As discussed in the previous response (Dec 2008), the present invention understands the importance of maintaining the integrity of the sample to not affect the classification of tumor cells, debris, or fragments. The present invention avoids the potential cell damage that would occur with an internal magnetic matrix by incorporating colloidal BSA-coated magnetite particles (80 to 130 nm, preferably 90-150 nm) with high gradient magnetic separation using and external field device (US20040181463, Page 6, Para 0072 and 0073).

Claims 44-46, 48, 49, 53-55 and 57-61 have been rejected under 35 USC 102(e) as being anticipated by Fodstad et al. (US Pat. No. 6,265,229).

Applicant has amended claims 44 and 53 to limit the method to colloidal paramagnetic particles as discussed above with an externally-applied high gradient magnetic field. The use of colloidal particles in this range has been shown to provide more complete mixing without significant damage to intact cells (US20040181463, Page 5, Para 0069). The particles described by Fodstad (i.e. Dynal beads) are considerably larger and thus have inherent problems with mixing. For example, the large magnetic particles are too large to diffuse effectively and will label target cells by collisions created by mixing. Consequently, mixing complete requires increased mixing times and larger amounts of magnetic particles added to the sample. These requirements add to the potential of cell damage and the generation of debris which ultimately affects the analysis. By incorporating these larger particles, Fodstad does not appreciate the mixing and cell damage problems associated with the analysis, which would be especially problematic in rare cell or debris collection. Applicant has limited the particle size to address both the Fodstad and Schmitz references.

Applicant respectfully requests that a timely Notice of Allowance be issued in this case.

Respectf ully submitted,

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